REMARKS

This paper is responsive to the Office Action dated November 18, 2003, which is the first action on the merits of the application. The Office Action was initially indicated as being made final, but the finality was subsequently removed, as acknowledged in the Communication mailed December 13, 2004.

Claims 73-104 were previously pending in the application; claims 75-78 73-86, 91-94 and 101-104 were under examination. Upon entry of this Amendment, claims 74, 79, 82, 87, 90, 95, and 97-100 are newly canceled. Claims 73, 80, 81, 88, 89, and 96 are still pending, but withdrawn from examination. Claims 75-78, 83-86, 91-94, and 101-104 have been variously amended and are under examination.

Entry of the claim amendments does not introduce new matter into the disclosure. Some claims have been rewritten in independent form, and some changes have been made to state explicitly what was previously inherent in the claim wording. Coverage is maintained for all equivalents of the claimed subject matter for which applicants were previously entitled.

Further consideration and allowance of the application is respectfully requested.

Interview summary:

The undersigned thanks Examiner Bradley L. Sisson, Ph.D., for the courtesy of telephone interviews on March 8 and March 15, 2004. The interviews were congenial and constructive. Various aspects of the Office Action and several possible claim amendments were discussed. The undersigned did not acquiesce that the statement at page 282 of the specification has no effect, but indicated that applicants need not rely on the statement for prosecution of the application. The 35 USC § 112 ¶ 1 rejection was discussed, and the Examiner made many helpful suggestions for remarks that applicants could put forward to address the issues raised.

Specification

The title has been amended, as suggested.

The statement on page 282 of the specification has not been altered, as applicants are not required to do so. The application as filed fulfills all the patentability requirements of 35 USC §§ 101, 102, 103, and 112 for the claims under examination. The claimed invention is new, non-obvious, has utility, and is fully described and enabled by the specification as filed, when read in the context of what was known to those skilled in the art at the time of filing.

Double Patenting:

Claims 74-78, 83-86, and 91-94 stand rejected for obviousness-type double patenting with respect to claims 1-8 of U.S. Patent No. 6,475,789, claims 3-10 of U.S. Patent No. 6,261,836, and claim 1 of U.S. Patent No. 6,093,809.

Applicants do not agree that the "fragment" referred to in the claims as previously presented included peptides of a single amino acid in length. The subject matter claimed in the '809 patent relates to a telomerase protein of a non-mammalian species, and does not meet the identity requirements of the invention claimed here.

With regards to the '789 and '836 patents, applicants undertake to file terminal disclaimers or appropriately address the double patenting issue once the Office indicates that the invention claimed in the present application is otherwise deemed in condition for allowance.

Rejections under 35 USC § 112 ¶ 1 and § 101:

Claims 75-78, 83-86 and 91-94 stand rejected as failing to comply with the written description requirement of § 112 ¶ 1. The Office Action indicates that the claims can be read so that the variant or fragment referred to encodes a single amino acid.

The claims as previously presented were worded in such a way that the claimed variant or fragment also retained the property of having *telomerase activity when complexed with telomerase RNA.*

By way of this amendment, the language of the claim has now been simplified to remove reference to variants or fragments. In fact, these terms are not needed, because the claimed polynucleotide encodes various TRT proteins defined in structural terms. Claim 75 indicates that the protein contains a sequence *that is at least 80% identical to SEQ. ID NO:2.* Similarly, claim 83 indicates that the protein contains a sequence that is at least 90% identical to SEQ. ID NO:2.

Claim 91 indicates that the protein contains a sequence that is at least 80% identical to 500 contiguous amino acids of SEQ. ID NO:2. The TRT protein is also functionally defined as having telomerase activity when complexed with telomerase RNA. These claims therefore encompass not only the native human TRT sequence, but also homologs that fall within the scope of the structural identity required — *providing* that the functional activity is also present.

It is clear that these claims do not read on polynucleotides that encode short peptide sequences. For example, in claim 75, the protein contains a sequence that is at least 80% identical to SEQ. ID NO:2. Furthermore, because of the functional requirement for telomerase activity, the protein will also contain all the structural features of the molecule required to provide the activity. As discussed extensively in the specification, these features are distributed extensively across the length of the TRT protein.

The form of the pending claims is in compliance with the USPTO Training Materials for the Written Description Guidelines, promulgated by the Patent Office on March 7, 2000. See especially Example 14, which claims protein variants based on identity with a single prototype sequence, in conjunction with a specific functional activity. This complies with the written description requirements for DNA and protein sequences as required by the standard required by *Regents of University of California v.Eli Lilly & Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997).

The specification provides a number of assays for determining telomerase activity, as recited in the claim. One skilled in the art may readily make variants of SEQ. ID NO:2 by introducing mutations by standard techniques, and then testing the mutants for telomerase activity according to the assay. The specification provides considerable guidance as to where to make alterations in the structure when making variants. The human TRT sequence is compared with other reverse transcriptases, and the motif structure of TRT is explained in considerable detail (e.g., Figures 2 and 4). The user may be guided by the motif structure in making variants if they like, or simply use a random mutation strategy followed by functional testing.

The standard texts *Protocols in Molecular Biology* (Ausubel et al. eds.) and *Molecular Cloning: A Laboratory Manual* (Sambrook et al. eds.), which were published before the priority application was filed, describe techniques employing chemical mutagenesis, cassette mutagenesis, degenerate oligonucleotides, mutually priming oligonucleotides, linker-scanning mutagenesis, alanine-scanning mutagenesis, and error-prone PCR. Other efficient methods include the E. coli mutator strains of Stratagene (Greener et al., Methods Mol. Biol. 57:375, 1996) and the DNA shuffling technique of Maxygen (Patten et al., Curr. Opin. Biotechnol. 8:724, 1997; Harayama, Trends

Biotechnol. 16:76, 1998). Kits and reagents for performing mutagenesis according to these techniques are available commercially from these and other companies.

Mutagenized variants can then be cloned out and tested for functionality as described in the specification. The example section provides assays for determining telomerase activity, and there were other assays for telomerase known at the time this application was filed: for example, measuring telomere length when TRT is transfected into cells, or measuring extension of telomeric primers by dot blot, reverse transcription, or by the telomerase repeat amplification protocol. The functional variants are selected for use according to the invention, or subjected to further rounds of mutation and functional selection to obtain the degree of variation desired.

Accordingly, the scope of the claimed invention is fully described by the specification, as it would be understood by those skilled in the art at the time of filing of the priority application. The full scope of the claimed invention can be practiced by the skilled reader without undue experimentation.

Applicants respectfully submit that the scope of the invention claimed in this application is appropriate and necessary to protect and commercialize this invention. It took enormous effort and ingenuity to obtain the human TRT sequence (SEQ. ID NO:2). Now that it has been obtained, minor changes can be made to the sequence without adversely affecting function, as a matter of routine experimentation. Applicants should be entitled to claim scope that protects against competitors from making trivial variants of the prototype sequence.

The claimed invention meets the written description requirements of § 112 ¶ 1. It has commercial utility for extending proliferative capacity of cells for research and therapeutic purposes, as described extensively in the specification. Withdrawal of these rejections is respectfully requested.

Rejections under 35 USC § 102:

Certain claims stand rejected under § 102(b) as being anticipated by the information in a review article by Rhyu (J. Nat. Cancer Inst. 87:12, 1995).

The undersigned cannot identify any polynucleotide sequences in the article, except for telomere repeat sequences, and fragment sequences of the RNA component from the telomerase of *Tetrahymena*, a single cell ciliate. None of these sequences appear to encode any protein at all. They therefore cannot encode a protein that is 80% identical to human TRT, which has telomerase catalytic activity when complexed with telomerase RNA (claim 75). At the time the Rhyu article was published, telomerase reverse transcriptase (the protein component of the active telomerase holoenzyme) had not been obtained or characterized from any species, mammalian or otherwise.

Accordingly, the cited article does not anticipate the claimed invention. Withdrawal of this rejection is respectfully requested.

Request for Rejoinder:

Claims 80, 88, and 96 (Group V) are method claims that depend from and incorporate the limitations of product claims in the elected group (Group I).

Applicants hereby reiterate the request made on November 6, 2003, that these claims (and all other method claims depending from product claims in the elected group) be rejoined into the group under examination, upon determination that the product claims are patentable, in accordance with MPEP § 821.04.

Claims 73, 81, and 89 (Group I) are claims to TRT protein defined in the same manner as the TRT protein referred to and encoded by claims 75, 83, and 91. In order to determine that the polynucleotides of the elected group are free of prior art, the Office has already searched SEQ. ID NO:2. Rejoinder of Group I into the group under examination was made in the response filed November 6, 2003.

MPEP § 803 prohibits the Office from restricting different embodiments of an invention where there would be no burden on the Examiner to examine the claims together — irrespective of whether the embodiments are patentably distinct. This application claims priority to USSN 08/854,050, which issued as U.S. Patent 6,261,836 on July 17, 2001. Since the claims in Groups I and II have already been fully searched in both the priority and the instant application, it imposes no burden to have them rejoined together into the group under examination.

Rejoinder and allowance of all pending claims in the application is respectfully requested.

Disclosure under 37 CFR § 1.56:

U.S. Patent No. 6,337,200 issued on January 8, 2002. It was invented by Gregg Morin at Geron Corporation, and claims functional variants of human telomerase reverse transcriptase. The patent has a first priority filing date of March 31, 1998. The '200 patent is not prior art to the invention claimed here. The present application is a continuation of USSN 08/974,549 (now U.S. Patent No. 6,166,178), which was filed on November 19, 1997.

PATENT
USSN 09/721,506
002616US; 018-210c

Request for Interview

Applicants respectfully request that all outstanding rejections be reconsidered and withdrawn. The application is believed to be in condition for allowance, and a prompt Notice of Allowance is requested.

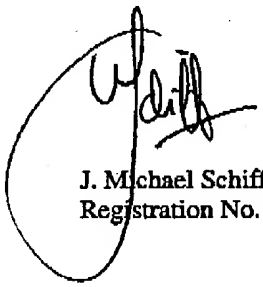
In the event that the Examiner determines that there are other matters to be addressed, applicants hereby request an interview by telephone.

Fees Due

The accompanying papers authorize the Commissioner to charge the Deposit Account for the extension of time, and three new independent claims.

Should the Patent Office determine that payment of any other fees are required at this time for further consideration of this application, applicants authorize the Commissioner to charge the cost of such fees to Deposit Account No. 07-1139, referencing the docket number indicated above.

Respectfully submitted,



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